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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,882	11/04/2003	Robert C. Brunham	1038-1274 MIS:jb	7783

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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 05/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/699,882	BRUNHAM ET AL.	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-32 and 34-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-32 and 34-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/28/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 29-32 and 34-40 are pending.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

1. The information disclosure statement filed October 28, 2004 has been considered.

Rejections Withdrawn

2. The Obviousness type double patenting rejection is herein withdrawn in light of Applicant's traversal and the restriction requirement made in the Parent Application.

Rejections Maintained

1. Claims 29,35,37-40 rejected under 35 U.S.C. 102(e) as being anticipated by Gurtiss III (US Pat. 5,389,368), is maintained for reasons of record in paper number 10152004, and responses set forth below.

2. Claims 30-32 ,34 and 36 rejected under 35 U.S.C. 103(a) as being unpatentable over Gurtiss, III (US Pat. 5,389,368) as applied to claims 29,35,37-40 above, in view of Burnham (WO98/02546), is maintained for reasons of record in paper number 10152004, and responses set forth below.

Response to Arguments

3. Applicant's arguments filed January 21, 2005 have been fully considered but they are not persuasive.

4. The rejection of claims 29,35,37-40 rejected under 35 U.S.C. 102(e) as being anticipated by Gurtiss III (US Pat. 5,389,368 is traversed on the grounds that the primary immunization of

claim 29 is effected by administration of an attenuated bacterial vector that comprises a plasmid DNA which is released into the cytoplasm of the infected host cells and the encoded gene expressed in the host cells (Remarks/Arguments page 3, paragraph 2).

5. It is the position of the examiner that Gurtiss III (US Pat. 5,389,368) disclose Salmonella typhimurium, S. typhi and other Salmonella species to evidence the ability to attach to, invade and proliferate in the cells of the gut-associated lymphoid tissue (GALT; Peyer's Patches) (Carter and Collins, J. Exp. Med. 139: 1189-1203, (1974)) (see US Pat. 5,389,368: col. 1, lines 66-68 and col. 2, lines 1-18), thus the Chlamydia protein (Gurtiss III, claim 6) is expressed in the eukaryotic host cell, as Salmonella is an intracellular pathogen. Inherently the reference anticipates the instantly claimed invention because Salmonella-mediated delivery of a nucleic acid molecule encoding a Chlamydia antigen to the GALT elicits an immune response because the avirulent Salmonella mutants have lost the ability to cause disease without impairment in their ability to attach to and invade the GALT , and the instantly claimed invention has not been distinguished from the invention of Gurtiss III, US Pat. 5,389,368.

6. With respect Applicant's statement that the allowed application, now US Pat. 6,676,949, was issued over the US Pat. 5,389,368 Patent and the instantly pending claims also define over the applied reference,

7. It is the position of the examiner that the allowed claims are directed to method claims that comprise first and second administrations, specifically the attenuated bacterium followed by a second administration of Chlamydial antigen. The allowed claims are also directed to the administration of an attenuated bacteria/vector that encodes a MOMP protein, wherein the

instantly claimed attenuated bacterial/vector encodes any Chlamydial protein that will induce an immune response. What is now claimed only requires a single administration step, of an attenuated bacterium that encodes any Chlamydial protein and the allowed claims are directed to the administration of an attenuated bacterium that encodes Chlamydia MOMP protein. Applicant's traversal is not commensurate in scope with the instantly claimed invention.

8. Applicant's representative asserts that "it is the promoter in the DNA construct that directs the expression of the MOMP in the host cells only and not in the attenuated bacteria."

9. It is the position of the examiner that Gurtiss teaches attenuated Salmonella strains as carriers (see col. 8, line 49; col. 10, lines 10-12) for a vector (see col 9, lines 29-35) that contains a nucleic acid that encodes a Chlamydia trachomatis antigen(Gurtiss, claim 6) and the expression of the encoded gene product is accomplished by a promoter operatively coupled to the nucleic acid in the expression vector (see col.11, lines 39-45; col. 26, lines 6-22; Tables 1, col. 16, Table 10, col. 28). Salmonella are invasive bacteria and would express the vector upon entry into the animal host cells. The attenuated Salmonella of Gurtiss would express the carried vector in the host cells. Applicant's arguments are not commensurate in scope with what is now claimed in claims 29,35,37-40, the claims against which Gurtiss, III was applied. While claim 36 recites the species of Chlamydial antigen MOMP, Gurtiss III was not applied under 35 USC 102 against claim 36, and the Salmonella strains are considered to be carrier strains of attenuated bacteria for the expression of a heterologous immunogen in a host cell, specifically the cells of the host GALT.

10. The rejection of claims 30-32 ,34 and 36 rejected under 35 U.S.C. 103(a) as being unpatentable over Gurtiss, III (US Pat. 5,389,368) as applied to claims 29,35,37-40 above, in view of Burnham (WO98/02546), is traversed on the grounds that "the Examiner does not refer to any teaching of Brunham which would remedy the basic defects of Gurtiss as discussed above.

11. It is the position of the examiner that Burnham describes additional means for the expression of a Chlamydial antigen in a host cell, wherein Gurtiss III described an attenuated Salmonella typhimurium bacteria harboring an expression vector that comprised a nucleic acid molecule encoding a Chlamydial antigen, wherein the attenuated carrier Salmonella strain expressed the nucleic acid gene product (see Gurtiss III, col. 6, line 18; col. 8, lines 49-51 and col. 9, lines 47-48) intracellularlly for induction of an immune response and Burnham described a species of Chlamydial antigen coding sequence, specifically the nucleic acid that encodes a MOMP protein from trachomatis under the control of a cytomegalovirus promoter placed in the plasmid vector is pcDNA3.

12. Brunham was applied in combination with Gurtiss III because the two references are analogous art in teaching nucleic acid molecules that encode Chlamydia antigens in vectors, and Burnham teaches a species of protective Chlamydial MOMP or MOMP fragment antigen thereof obtained from Chlamydia trachomatis, and incorporated the nucleic acid into a plasmid that comprised a cytomegalovirus promoter for expression of MOMP therefrom, (see Burnham, page 25, Table 2; and claims 4, 6, 16). No unexpected results have been made of record to obviate the rejection of Gurtiss III in view of Brunham. The rejection is maintained for reasons of record and responses set forth above.

The effective expression of a protein is taught to be associated with utilization of a promoter in an attenuated Salmonella containing an expression vector (see col. 26, lines 8-13).

Gurtiss clearly teaches a method of immunizing that comprises the steps of initially administering to a host an attenuated bacterium that comprises a vector that encodes a Chlamydia gene product (protein), with subsequent administration of purified gene product (protein).

Brunham teaches a specific nucleic acid that encodes Chlamydia (pneumoniae and trachomatis) antigen and utilization of a cytomegalovirus promoter for the production of a bivalent vaccine (see Brunham, page 13, lines 20-24).

1. It is asserted by Applicant that the Gurtiss reference was written before the days of the contemplation of DNA immunization, there can be no contemplation of in vivo heterologous gene expression" and that Gurtiss "simply describes recombinant DNA techniques as they existed at the time of Gurtiss for in vitro heterologous gene expression.

2. It is the position of the examiner that Gurtiss teaches the in vivo expression of a heterologous nucleic acid in an attenuated bacteria that is in host cells. The expression of the nucleic acid molecule takes place in host cells based upon the expression vector in the attenuated bacteria.

Applicant has not claimed a method of DNA immunization of a immunocompetent animal, but claims a method of stimulating an immune response utilizing an attenuated bacteria that expresses a heterologous coding sequence for a protein. There is no requirement that the host cells to be transformed, but only that the vector find expression in host cells.

Two types of host cells are recited in the claims, bacterial host cell and host host cells. Salmonella is a host cell that replicates in animal host cells, which results in the induction of the vector encoded nucleic acid molecule expression in the host cells. Applicant's arguments are not commensurate in scope with the claimed invention.

3. Applicant states "It is submitted that the Examiner is incorrect in this regard and the only "host cell" expression which is discussed in Gurtiss is expression in the avirulent bacteria itself and not any other "host cell."

4. It is the position of the examiner that the claimed invention is not required to transform the host animal cells, as claim 29 does not recite essential vector components for the transformation of host animal cells, but claims the administration of attenuated bacterial host cells that would express the encoded vector coupled nucleic acid upon invasion of host animal cells. The expression of the encoded nucleic acid molecule would be in animal host cells that have been invaded by the attenuated bacteria. Salmonella is an invasive bacteria, the attenuated strains of Gurtiss are taught to be invasive attenuated strains, and the vector would find expression in the host cells, upon the attenuated Salmonella invading the cell.

5. It is argued the Examiner cannot equate the "host cells" in Gurtiss, which are bacterial cells, with the host cells in claim 29, which are eukaryotic cells.

6. It is the position of the examiner that at no time were prokaryotic equated with eukaryotic cells. Claim 29 does not recite the term eukaryotic cells, but it is implied because no prokaryotic cells are known to produce an immune response. The bacterial host cells of Gurtiss

invade the animal host cells to induce an immune response. The expression of encoded nucleic acid molecules is accomplished by the attenuated salmonella bacteria upon invasion of animal host cells. The attenuated salmonella bacterial host cell expresses the antigen in animal host cells upon invasion of the host cell. Brunham was cited for teaching specific Chlamydia nucleic acid molecules and a specific promoter that is taught to be combinable to form a vaccine that contains antigenic material from more than one pathogen (see page 13, lines 19-24). Brunham teaches the incorporation of a promoter and Chlamydia nucleic acid molecule into a plasmid vector with subsequent incorporation into an attenuated E.coli bacterial strain (see page 17, lines 3-7). Brunham showed that the combination of a promoter/MOMP nucleic acid molecule/ vector/attenuated bacteria composition is readily made.

Gurtiss, III provides motivation to combine the promoter/MOMP nucleic acid molecule/vector of Brunham with the Salmonella of Gurtiss, III because the attenuated Salmonella serves to carry the encoded nucleic acid molecule in a host cell for immunizing a host (see col. 34, lines 32-39; col. 35, line 8), and provides sight directed vector delivery system to host cells (see col. 8, lines 47-51; col. 7, lines 27-29). The attenuated Salmonella minimizes possible random adsorption of nucleic acid molecules, maximizes stimulation of a mucosal immune response (Salmonella binds to GALT and BALT cells) in mucosal host cells and can stimulate an immune response to Salmonella, as well as the heterologous protein expressed in the host cells. Brunham shows a highly versatile promoter that successfully functioned to express a Chlamydia MOMP protein in transformed host cells which resulted in stimulating an immune response and would be combinable with the bacterial host cells of Gurtiss. (Brunham page 13, line 14). See *In re Fine*, 837 F.d. 1071, 5 USPQ2d 1596 (Fed. Cir 1988)and *In re Jones*,

958 F.d. 347, 21 USPQ2d 1941 (Fed. Cir. 1992). The claims are obviated by Gurtiss in view of Brunham for reasons of record and responses set forth above.

Conclusion

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
May 2, 2005

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